

General

Guideline Title

Guidelines for the prevention of stroke in women: a statement for healthcare professionals from the American Heart Association/American Stroke Association.

Bibliographic Source(s)

Bushnell C, McCullough LD, Awad IA, Chireau MV, Fedder WN, Furie KL, Howard VJ, Lichtman JH, Lisabeth LD, Piña IL, Reeves MJ, Rexrode KM, Saposnik G, Singh V, Towfighi A, Vaccarino V, Walters MR, on behalf of the American Heart Association Stroke Council, Council on Cardiovascular and Stroke Nursing, Council on Clinical Cardiology, Council on Epidemiology and Prevention, Council for High Blood Pressure Research. Guidelines for the prevention of stroke in women: a statement for healthcare professionals from the American Heart Association/American Stroke Association. Stroke. 2014 May;45(5):1545-88. [449 references] PubMed

Guideline Status

This is the current release of the guideline.

Recommendations

Major Recommendations

Definitions for the levels of the evidence (A-C) and classes of recommendations (I-III) are provided at the end of the "Major Recommendations" field.

Sex-Specific Risk Factors

Preeclampsia and Pregnancy Outcomes

Prevention of Preeclampsia

- 1. Women with chronic primary or secondary hypertension or previous pregnancy-related hypertension should take low-dose aspirin from the 12th week of gestation until delivery (Class I; Level of Evidence A).
- 2. Calcium supplementation (of≥1 g/d, orally) should be considered for women with low dietary intake of calcium (<600 mg/d) to prevent preeclampsia (Class I; Level of Evidence A).

Treatment of Hypertension in Pregnancy and Postpartum

- 1. Severe hypertension in pregnancy should be treated with safe and effective antihypertensive medications, such as methyldopa, labetalol, and nifedipine, with consideration of maternal and fetal side effects (Class I; Level of Evidence A).
- 2. Consideration may be given to treatment of moderate hypertension in pregnancy with safe and effective antihypertensive medications, given the evidence for possibly increased stroke risk at currently defined systolic and diastolic blood pressure (BP) cutoffs, as well as evidence for decreased risk for the development of severe hypertension with treatment (although maternal-fetal risk-benefit ratios have not been established) (Class IIa; Level of Evidence B).
- 3. Atenolol, angiotensin receptor blockers, and direct renin inhibitors are contraindicated in pregnancy and should not be used (Class III; Level of Evidence C).
- 4. After giving birth, women with chronic hypertension should be continued on their antihypertensive regimen, with dosage adjustments to reflect the decrease in volume of distribution and glomerular filtration rate that occurs after delivery. They should also be monitored carefully for the development of postpartum preeclampsia (Class IIa; Level of Evidence C).

Prevention of Stroke in Women with a History of Preeclampsia

1. Because of the increased risk of future hypertension and stroke 1 to 30 years after delivery in women with a history of preeclampsia (Level of Evidence B), it is reasonable to (1) consider evaluating all women starting 6 months to 1 year postpartum, as well as those who are past childbearing age, for a history of preeclampsia/eclampsia and document their history of preeclampsia/eclampsia as a risk factor, and (2) evaluate and treat for cardiovascular risk factors including hypertension, obesity, smoking, and dyslipidemia (Class IIa; Level of Evidence C).

Cerebral Venous Thrombosis (CVT)

- 1. In patients with suspected CVT, routine blood studies consisting of a complete blood count, chemistry panel, prothrombin time, and activated partial thromboplastin time should be performed (Class I; Level of Evidence C).
- 2. Screening for potential prothrombotic conditions that may predispose a person to CVT (e.g., use of contraceptives, underlying inflammatory disease, infectious process) is recommended in the initial clinical assessment (Class I; Level of Evidence C).
- 3. Testing for prothrombotic conditions, including protein C, protein S, or antithrombin deficiency; antiphospholipid syndrome; prothrombin G20210A mutation; and factor V Leiden can be beneficial for the management of patients with CVT. Testing for protein C, protein S, and antithrombin deficiency is generally indicated 2 to 4 weeks after completion of anticoagulation. There is a very limited value of testing in the acute setting or in patients taking warfarin (Class IIa; Level of Evidence B).
- 4. In patients with provoked CVT (associated with a transient risk factor), vitamin K antagonists may be continued for 3 to 6 months, with a target international normalized ratio of 2.0 to 3.0 (Class IIb; Level of Evidence C).
- 5. In patients with unprovoked CVT, vitamin K antagonists may be continued for 6 to 12 months, with a target international normalized ratio of 2.0 to 3.0 (Class IIb; Level of Evidence C).
- 6. For patients with recurrent CVT, venous thromboembolism (VTE) after CVT, or first CVT with severe thrombophilia (i.e., homozygous prothrombin G20210A; homozygous factor V Leiden; deficiencies of protein C, protein S, or antithrombin; combined thrombophilia defects; or antiphospholipid syndrome), indefinite anticoagulation may be considered, with a target international normalized ratio of 2.0 to 3.0 (Class IIb; Level of Evidence C).
- 7. For women with CVT during pregnancy, low-molecular-weight heparin (LMWH) in full anticoagulant doses should be continued throughout pregnancy, and LMWH or vitamin K antagonist with a target international normalized ratio of 2.0 to 3.0 should be continued for ≥6 weeks postpartum (for a total minimum duration of therapy of 6 months) (Class I; Level of Evidence C).
- 8. It is reasonable to advise women with a history of CVT that future pregnancy is not contraindicated. Further investigations regarding the underlying cause and a formal consultation with a hematologist or maternal fetal medicine specialist are reasonable (Class IIa; Level of Evidence B).
- 9. It is reasonable to treat acute CVT during pregnancy with full-dose LMWH rather than unfractionated heparin (Class IIa; Level of Evidence C).
- 10. For women with a history of CVT, prophylaxis with LMWH during future pregnancies and the postpartum period is reasonable (Class IIa; Level of Evidence C).

Oral Contraceptives (OCs)

- 1. OCs may be harmful in women with additional risk factors (e.g., cigarette smoking, prior thromboembolic events) (Class III; Level of Evidence B) (Kemmeren et al., 2002; Slooter et al., 2005).
- 2. Among OC users, aggressive therapy of stroke risk factors may be reasonable (Class IIb; Level of Evidence C) (Kemmeren et al., 2002; Slooter et al., 2005; Bousser et al., 2000).
- 3. Routine screening for prothrombotic mutations before initiation of hormonal contraception is not useful (Class III; Level of Evidence A) (Wu et al., 2006).
- 4. Measurement of BP before initiation of hormonal contraception is recommended (Class I; Level of Evidence B) (World Health Organization, 1996; Tepper et al., 2013; Heinemann et al., 1998).

Menopause and Postmenopausal Hormone Therapy (HT)

Postmenopausal HT

- 1. HT (conjugated equine estrogen [CEE] with or without medroxyprogesterone) should not be used for primary or secondary prevention of stroke in postmenopausal women (Class III; Level of Evidence A).
- 2. Selective estrogen receptor modulators, such as raloxifene, tamoxifen, or tibolone, should not be used for primary prevention of stroke (Class III; Level of Evidence A).

Risk Factors More Common in Women Than Men

Migraine with Aura

- 1. Because there is an association between higher migraine frequency and stroke risk, treatments to reduce migraine frequency might be reasonable, although evidence is lacking that this treatment reduces the risk of first stroke (Class IIb; Level of Evidence C).
- 2. Because of the increased stroke risk seen in women with migraine headaches with aura and smoking, it is reasonable to strongly recommend smoking cessation in women with migraine headaches with aura (Class IIa; Level of Evidence B).

Obesity, Metabolic Syndrome, and Lifestyle Factors

1. A healthy lifestyle consisting of regular physical activity, moderate alcohol consumption (<1 drink/d for nonpregnant women), abstention from cigarette smoking, and a diet rich in fruits, vegetables, grains, nuts, olive oil, and low in saturated fat (such as the DASH [Dietary Approaches to Stop Hypertension] diet) is recommended for primary stroke prevention in women with cardiovascular risk factors (Class I; Level of Evidence B).

2. Lifestyle interventions focusing on diet and exercise are recommended for primary stroke prevention among individuals at high risk for stroke (Class I; Level of Evidence B).

Atrial Fibrillation (AF)

- 1. Risk stratification tools in AF that account for age- and sex-specific differences in the incidence of stroke are recommended (Class I; Level of Evidence A).
- 2. Considering the increased prevalence of AF with age and the higher risk of stroke in elderly women with AF, active screening (in particular of women >75 years of age) in primary care settings using pulse taking followed by an electrocardiogram (ECG) as appropriate is recommended (Class I; Level of Evidence B).
- 3. Oral anticoagulation in women aged ≤65 years with AF alone (no other risk factors; women with Cardiac failure, Hypertension, Age, Diabetes Stroke system [CHADS₂]=0 or Congestive heart failure, Hypertension, Age ≥75 years, Diabetes mellitus, Stroke, Vascular disease, Age 65-74 years, Sex category [CHA₂DS₂-VASc]=1]) is not recommended (Class III; Level of Evidence B). Antiplatelet therapy is a reasonable therapeutic option for selected low-risk women (Class IIa; Level of Evidence B).
- 4. New oral anticoagulants are a useful alternative to warfarin for the prevention of stroke and systemic thromboembolism in women with paroxysmal or permanent AF and prespecified risk factors (according to CHA₂DS₂-VASc) who do not have a prosthetic heart valve or hemodynamically significant valve disease, severe renal failure (creatinine clearance 15 mL/min), lower weight (<50 kg), or advanced liver disease (impaired baseline clotting function) (Class I; Level of Evidence A).</p>

Strategies for Prevention of Stroke: Are They Different in Women?

Strategies for Prevention of Stroke in Women

- 1. Women with asymptomatic carotid stenosis should be screened for other treatable risk factors for stroke, and appropriate lifestyle changes and medical therapies should be instituted (Class I; Level of Evidence C) (Goldstein et al., 2011).
- 2. In women who are to undergo carotid endarterectomy (CEA), aspirin is recommended unless contraindicated, because aspirin was used in every major trial that demonstrated efficacy of CEA (Class I; Level of Evidence C).
- 3. Prophylactic CEA performed with <3% morbidity/mortality can be useful in highly selected patients with an asymptomatic carotid stenosis (minimum 60% by angiography, 70% by validated Doppler ultrasound) (Class IIa; Level of Evidence A).
- 4. For women with recent transient ischemic attack (TIA) or ischemic stroke (IS) within the past 6 months and ipsilateral severe (70%–99%) carotid artery stenosis, CEA is recommended if the perioperative morbidity and mortality risk is estimated to be <6% (Class I; Level of Evidence A) (Furie et al., 2011).
- 5. For women with recent TIA or IS and ipsilateral moderate (50%–69%) carotid stenosis, CEA is recommended depending on patient-specific factors, such as age and comorbidities, if the perioperative morbidity and mortality risk is estimated to be <6% (Class I; Level of Evidence B) (Furie et al., 2011).
- 6. When CEA is indicated for women with TIA or stroke, surgery within 2 weeks is reasonable rather than delaying surgery, if there are no contraindications to early revascularization (Class IIa; Level of Evidence B) (Furie et al., 2011).
- 7. Aspirin therapy (75–325 mg/d) is reasonable in women with diabetes mellitus unless contraindicated (Class IIa; Level of Evidence B) (Mosca et al., 2011).
- 8. If a high-risk (i.e., 10-year predicted CVD risk ≥10%) woman has an indication for aspirin but is intolerant of aspirin therapy, clopidogrel should be substituted (Class I; Level of Evidence B) (Mosca et al., 2011).
- 9. Aspirin therapy can be useful in women ≥65 years of age (81 mg/d or 100 mg every other day) if BP is controlled and the benefit for IS and myocardial infarction (MI) prevention is likely to outweigh the risk of gastrointestinal bleeding and hemorrhagic stroke (Class IIa; Level of Evidence B) and may be reasonable for women <65 years of age for IS prevention (Class IIb; Level of Evidence B) (Mosca et al., 2011).

Definitions:

Applying Classification of Recommendations and Level of Evidence

		Size of Treatment Effect					
		CLASS I	CLASS IIa	SS IIa CLASS IIb	CLASS III No Benefit or Class III Harm		
		Benefit >>> Risk	Benefit >> Risk Additional studies	Benefit \geq Risk Additional studies with		Procedure/Test	Treatment
		Procedure/Treatment SHOULD be performed/ administered with focused objectives needed IT IS REASONABLE	broad objectives needed; additional registry data would be helpful	COR III: No Benefit	Not helpful	No proven benefit	
			to perform procedure/administer treatment	Procedure/Treatment MAY BE CONSIDERED	COR III: Harm	Excess cost without benefit or harmful	Harmful to patients
Estimate of Certainty (Precision) of Treatment	LEVEL A Multiple populations evaluated*	Recommendation that procedure or treatment is useful/effective Sufficient evidence from	Recommendation in favor of treatment or procedure being useful/effective Some conflicting	Recommendation's usefulness/efficacy less well established Greater conflicting evidence from	Recommendation that procedure or treatment is not useful/effective and may be harmful Sufficient evidence from multiple randomized trials or meta-analyses		

Effect	Data derived from multiple	multiple randomized trials	evidence from Size	of Treatment Effect	
	randomized clinical trials or meta-analyses	or meta-analyses	randomized trials or meta-analyses	or meta-analyses	
	LEVEL B Limited populations evaluated* Data derived from a single randomized trials or nonrandomized studies	Recommendation that procedure or treatment is useful/effective Evidence from single randomized trial or nonrandomized studies	Recommendation in favor of treatment or procedure being useful/effective Some conflicting evidence from single randomized trial or nonrandomized studies	 Recommendation's usefulness/efficacy less well established Greater conflicting evidence from single randomized trial or nonrandomized studies 	Recommendation that procedure or treatment is not useful/effective and may be harmful Evidence from single randomized trial or nonrandomized studies
	LEVEL C Very limited populations evaluated* Only consensus opinion of experts, case studies, or standard of care	 Recommendation that procedure or treatment is useful/effective Only expert opinion, case studies, or standard of care 	 Recommendation in favor of treatment or procedure being useful/effective Only diverging expert opinion, case studies, or standard of care 	 Recommendation's usefulness/efficacy less well established Only diverging expert opinion, case studies, or standard of care 	 Recommendation that procedure or treatment is not useful/effective and may be harmful Only expert opinion, case studies, or standard of care

A recommendation with Level of Evidence B or C does not imply that the recommendation is weak. Many important clinical questions addressed in the guidelines do not lend themselves to clinical trials. Although randomized trials are unavailable, there may be a very clear clinical consensus that a particular test or therapy is useful or effective.

Definition of Levels of Evidence Used in American Heart Association/American Stroke Association (AHA/ASA) Recommendations

Therapeutic	Therapeutic Recommendations			
Level of Evidence A	Data derived from multiple randomized clinical trials or meta-analyses			
Level of Evidence B	Data derived from a single randomized trial or nonrandomized studies			
Level of Evidence C	Consensus opinion of experts, case studies, or standard of care			
Diagnostic R	ecommendations			
Level of Evidence A	Data derived from multiple prospective cohort studies using a reference standard applied by a masked evaluator			
Level of Evidence B	Data derived from a single grade A study or 1 or more case-control studies, or studies using a evaluator			
Level of Evidence C	Consensus opinion of experts			

Definition of Classes of Recommendations Used in American Heart Association/American Stroke Association (AHA/ASA) Recommendations

Class I	Conditions for which there is evidence for and/or general agreement that the procedure or treatment is useful and effective.
Class II	Conditions for which there is conflicting evidence and/or a divergence of opinion about the usefulness/efficacy of a procedure or treatment.
Class IIa	The weight of evidence or opinion is in favor of the procedure or treatment.
Class IIb	Usefulness/efficacy is less well established by evidence or opinion.
Class III	Conditions for which there is evidence and/or general agreement that the procedure or treatment is not useful/effective and in some cases may be harmful.

^{*}Data available from clinical trials or registries about the usefulness/efficacy in different subpopulations, such as sex, age, history of diabetes, history of prior myocardial infarction, history of heart failure, and prior aspirin use.

Clinical Algorithm(s)

None provided

Scope

Disease/Condition(s)

- Ischemic stroke
- Hemorrhagic stroke
 - Intracerebral
 - Subarachnoid

Other Disease/Condition(s) Addressed

- Atrial fibrillation
- Carotid stenosis
- Cerebral venous thrombosis
- Migraine headaches

Guideline Category

Prevention

Risk Assessment

Screening

Treatment

Clinical Specialty

Cardiology

Family Practice

Internal Medicine

Neurology

Obstetrics and Gynecology

Preventive Medicine

Intended Users

Advanced Practice Nurses

Health Care Providers

Nurses

Physician Assistants

Physicians

Guideline Objective(s)

- To summarize data on stroke risk factors that are unique to and more common in women than men and to expand on the data provided in prior stroke guidelines and cardiovascular prevention guidelines for women
- To provide a new stroke prevention guideline that covers topics specific to women in more detail than has been included in current primary and secondary stroke prevention guidelines and provides more emphasis on stroke-specific issues in women than are included in the current cardiovascular prevention guideline for women
- To review risk factors that are unique to women or might affect women's risk of stroke differentially, as well as to determine whether there is a need for a
 stroke risk score for women that incorporates female-specific factors such as reproductive and menopausal factors

Target Population

Women with risk factors for stroke

Interventions and Practices Considered

- 1. Prevention and management of stroke risk factors
 - Prevention of preeclampsia
 - Low-dose aspirin
 - Calcium supplementation
 - Treatment of hypertension in pregnancy
 - Antihypertensive medications (e.g., methyldopa, labetalol, nifedipine), as indicated
 - Careful monitoring
 - · History of preeclampsia
 - Evaluation 6 months to 1 year postpartum
 - Treatment of cardiovascular risk factors
 - Cerebral venous thrombosis (CVT)
 - · Routine blood studies
 - Screening for prothrombotic conditions
 - · Vitamin K antagonists
 - Low-molecular weight heparin (LMWH)
 - Management during pregnancy
 - Oral contraceptives
 - Blood pressure (BP) measurement before initiation
 - Aggressive therapy of stroke risk factors
 - · Management of migraine with aura
 - Treatment to reduce migraine frequency
 - · Smoking cessation
 - Lifestyle interventions (e.g., diet, exercise) for obesity, metabolic syndrome, and lifestyle factors
 - Atrial fibrillation
 - Use of risk stratification tools (e.g., Cardiac failure, Hypertension, Age, Diabetes Stroke system [CHADS₂])
 - Screening in elderly women, especially women >75 years of age
 - Antiplatelet therapy
 - Oral anticoagulants in specific populations
- 2. Prevention strategies
 - Women with asymptomatic carotid stenosis
 - Screening for other treatable risk factors
 - · Lifestyle changes
 - Medical therapy
 - Prophylactic carotid endarterectomy (CEA)
 - · Aspirin therapy, as indicated
 - Clopidogrel if aspirin is not tolerated

Note: The following were considered but not recommended: routine screening for prothrombotic mutations before initiation of hormonal contraception, postmenopausal hormone therapy (HT) for prevention of stroke.

Major Outcomes Considered

- Recurrence rates
- · Morbidity and mortality
- Risk factors for stroke in women

- Cerebrovascular events
- Cardiovascular events

Methodology

Methods Used to Collect/Select the Evidence

Searches of Electronic Databases

Description of Methods Used to Collect/Select the Evidence

The authors searched Ovid MEDLINE, PubMed, Ovid MEDLINE in-process and other non-indexed citations, the CardioSource Clinical Trials Database (or similar database), the Cochrane Library, EMBASE, and Google scholar from 1990 through May 15, 2013. Inclusions were: (1) human subjects only; (2) articles published in English language; and (3) subjects ages 18 and over. Exclusions were: (1) no unpublished data (abstracts) unless presented at major national or international scientific meetings and cannot be older than 2 years; (2) Dissertations, books and conference proceedings are excluded.

Specific search terms used were oral contraceptives, contraceptive patch, vaginal ring, contraception, intrauterine device, menopause, postmenopausal hormone therapy, estrogen, progesterone, preeclampsia, eclampsia, gestational hypertension, chronic hypertension pregnancy, cerebral venous sinus thrombosis, thrombophilia, thromboembolism, migraine, migraine with aura, obesity, abdominal adiposity, body mass index, waist circumference, waist hip ratio, metabolic syndrome, physical activity, lifestyle change, depression, psychosocial stress, stroke clinical trials, cardiovascular clinical trials, asymptomatic carotid stenosis, symptomatic carotid stenosis, carotid angioplasty and stenting, carotid endarterectomy, aspirin, antiplatelet therapy, antithrombotic therapy, stroke risk score, stroke risk prediction, stroke, intracerebral, women, female, sex/gender specific/differences, atrial fibrillation, hemorrhagic/haemorrhagic stroke, subarachnoid, intracerebral, women, female, sex/gender specific/differences, trends, incidence, risk, prevalence, mortality, case-fatality, epidemiology, sex, female, gender, women, cerebrovascular, health care disparity, brain ischemia, hypertension, cerebral hemorrhage, intracranial hypertension.

Number of Source Documents

Not stated

Methods Used to Assess the Quality and Strength of the Evidence

Weighting According to a Rating Scheme (Scheme Given)

Rating Scheme for the Strength of the Evidence

Applying Classification of Recommendations and Level of Evidence

		Size of Treatment Effect					
		CLASS II CLASS III CLASS III		CLASS IIb	CLASS III <i>No Benefit</i> or Class III <i>Harm</i>		
		Benefit >>> Risk	Benefit >> Risk Additional studies	Benefit \geq Risk Additional studies with		Procedure/Test	Treatment
		Procedure/Treatment SHOULD be performed/ administered	IOULD be objectives needed formed/ ministered IT IS REASONABLE	broad objectives needed; additional registry data would be helpful	COR III: No Benefit	Not helpful	No proven benefit
			treatment MAY BE	Procedure/Treatment MAY BE CONSIDERED	COR III: Harm	Excess cost without benefit or harmful	Harmful to patients
Estimate of Certainty (Precision) of Treatment Effect	LEVEL A Multiple populations evaluated* Data derived from multiple randomized	Recommendation that procedure or treatment is useful/effective Sufficient evidence from multiple randomized trials or meta-analyses	 Recommendation in favor of treatment or procedure being useful/effective Some conflicting evidence from multiple randomized trials 	 Recommendation's usefulness/efficacy less well established Greater conflicting evidence from multiple randomized trials or meta-analyses 	tro m • Si	ecommendation that eatment is not useful/ ay be harmful ufficient evidence from ndomized trials or m	effective and multiple

clinical tri		or meta-analysesiz	e of Treatment Effect	
LEVEL I Limited population evaluated Data deriftom a sit randomiz trials or nonrando studies	that procedure or treatment is useful/effective * Evidence from single randomized trial or ed nonrandomized studies	Recommendation in favor of treatment or procedure being useful/effective Some conflicting evidence from single randomized trial or nonrandomized studies	 Recommendation's usefulness/efficacy less well established Greater conflicting evidence from single randomized trial or nonrandomized studies 	Recommendation that procedure or treatment is not useful/effective and may be harmful Evidence from single randomized trial or nonrandomized studies
Very limit population evaluated Only consensu opinion of experts, of studies, of standard care	that procedure or treatment is useful/effective Only expert opinion, case studies, or standard of care frease or	Recommendation in favor of treatment or procedure being useful/effective Only diverging expert opinion, case studies, or standard of care	 Recommendation's usefulness/efficacy less well established Only diverging expert opinion, case studies, or standard of care 	 Recommendation that procedure or treatment is not useful/effective and may be harmful Only expert opinion, case studies, or standard of care

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Level of Evidence B	Data derived from a single randomized trial or nonrandomized studies			
Level of Evidence C	Consensus opinion of experts, case studies, or standard of care			
Diagnostic R	decommendations			
Level of Evidence A	Data derived from multiple prospective cohort studies using a reference standard applied by a masked evaluator			
Level of Evidence B	Data derived from a single grade A study or 1 or more case-control studies, or studies using a evaluator			
Level of Evidence C	Consensus opinion of experts			

Methods Used to Analyze the Evidence

Review of Published Meta-Analyses

Systematic Review with Evidence Tables

Description of the Methods Used to Analyze the Evidence

The evidence is organized within the context of the American Heart Association (AHA) framework and is classified according to the joint AHA/American College of Cardiology and supplementary AHA Stroke Council methods of classifying the level of certainty and the class and level of evidence (see the "Rating Scheme for the Strength of the Evidence" field).

^{*}Data available from clinical trials or registries about the usefulness/efficacy in different subpopulations, such as sex, age, history of diabetes, history of prior myocardial infarction, history of heart failure, and prior aspirin use.

Methods Used to Formulate the Recommendations

Expert Consensus

Description of Methods Used to Formulate the Recommendations

Writing group members were nominated by the committee chair on the basis of their previous work in relevant topic areas and were approved by the American Heart Association (AHA) Stroke Council's Scientific Statement Oversight Committee and the AHA's Manuscript Oversight Committee. The panel reviewed relevant articles on adults using computerized searches of the medical literature through May 15, 2013.

Rating Scheme for the Strength of the Recommendations

Definition of Classes of Recommendations Used in American Heart Association/American Stroke Association (AHA/ASA) Recommendations

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Cost Analysis

The guideline developers reviewed published cost analyses.

Method of Guideline Validation

Internal Peer Review

Description of Method of Guideline Validation

The document underwent extensive American Heart Association (AHA) internal peer review, Stroke Council Leadership review, and Scientific Statements Oversight Committee review before consideration and approval by the AHA Science Advisory and Coordinating Committee.

This statement was approved by the American Heart Association Science Advisory and Coordinating Committee on December 13, 2013.

Evidence Supporting the Recommendations

References Supporting the Recommendations

Bousser MG, Conard J, Kittner S, de Lignieres B, MacGregor EA, Massiou H, Silberstein SD, Tzourio C. Recommendations on the risk of ischaemic stroke associated with use of combined oral contraceptives and hormone replacement therapy in women with migraine. Cephalalgia. 2000 Apr;20(3):155-6. PubMed

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Type of Evidence Supporting the Recommendations

The type of supporting evidence is identified and graded for each recommendation (see the "Major Recommendations" field).

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

Appropriate prevention of stroke in women

Potential Harms

- One of the seminal trials of primary prevention of cardiovascular disease (CVD), including stroke, in women is the Women's Health Study (WHS), a randomized trial of 100 mg of aspirin on alternate days versus placebo in 39,876 initially asymptomatic women 45 years of age, followed up for 10 years for a first major vascular event (nonfatal myocardial infarction [MI], nonfatal stroke, or cardiovascular death). An important adverse outcome, gastrointestinal hemorrhage requiring transfusion, was more frequent in the aspirin group (relative risk [RR], 1.40; 95% confidence interval [CI], 1.07–1.83; P=0.02 and absolute risk increase, 0.01% per year; number needed to harm, 10,000).
- Side effects of antihypertensive therapy tend to be encountered with a higher degree of frequency in women than men. Diuretic-induced disturbances of electrolyte concentration are seen more frequently in women, as is angiotensin-converting enzyme inhibitor—induced cough and calcium channel blocker (CCB)—related dependent edema.
- In subgroup analyses of some trials comparing medical management to carotid endarterectomy (CEA) in patients with symptomatic or asymptomatic carotid stenosis, women appeared to derive less benefit from surgery than men, potentially because of an increased risk of perioperative events; however, the data were inconclusive because of small sample sizes within sex strata and the post hoc nature of some of the analyses.
- New oral anticoagulants are a useful alternative to warfarin for the prevention of stroke and systemic thromboembolism; however, caution about overdosing
 must be used considering the additive effect of age, sex, renal function, and concomitant medications (acetylsalicylic acid, clopidogrel, nonsteroidal antiinflammatory drugs, P-glycoprotein inhibitors) in increasing the concentrations of new oral anticoagulants.
- See Table 4, "Summary of Antihypertensive Drugs Used During Pregnancy," in the original guideline document for the teratogenicity or fetal-neonatal adverse
 effects.

Contraindications

Contraindications

- Angiotensin-converting enzyme inhibitors, angiotensin receptor blockers, and direct renin inhibitors are contraindicated at all stages of pregnancy because of teratogenicity and adverse fetal outcomes.
- Migraine treatment with triptans is contraindicated in patients with a history of cerebrovascular disease or coronary heart disease, as explicitly stated in guidelines from the American Academy of Neurology.

Qualifying Statements

Qualifying Statements

- In this guideline, the Writing Group has summarized the current evidence and provided summaries and gaps for prevention focused on the risk factors that are either unique to or more common in women than men. Some of the recommendations in this guideline were formerly associated with other prevention guidelines but have been assimilated because of the focus on women. In addition, the Writing Group has summarized the data that support the development of woman-specific stroke risk profiles, which might more accurately reflect a woman's future risk of stroke than some of the currently available stroke risk profiles.
- Prevention efforts for women would be enhanced if future epidemiological studies provided more detail on stroke subtype, especially hemorrhagic stroke, in
 addition to accounting for age and sex. Similarly, it is important to improve stroke awareness and provide more rigorous education to women at younger
 ages, including childbearing ages, because of women's increased risk of stroke with age; the risks of stroke associated with pregnancy, gestational
 hypertension, and hormonal contraception; and the onset of stroke risk factors such as obesity, hypertension, and diabetes mellitus, which occur at younger
 ages.

Implementation of the Guideline

Description of Implementation Strategy

An implementation strategy was not provided.

Implementation Tools

Patient Resources

Resources

Staff Training/Competency Material

For information about availability, see the Availability of Companion Documents and Patient Resources fields below.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

Living with Illness

Staying Healthy

IOM Domain

Effectiveness

Patient-centeredness

Identifying Information and Availability

Bibliographic Source(s)

Bushnell C, McCullough LD, Awad IA, Chireau MV, Fedder WN, Furie KL, Howard VJ, Lichtman JH, Lisabeth LD, Piña IL, Reeves MJ, Rexrode KM, Saposnik G, Singh V, Towfighi A, Vaccarino V, Walters MR, on behalf of the American Heart Association Stroke Council, Council on Cardiovascular and Stroke Nursing, Council on Clinical Cardiology, Council on Epidemiology and Prevention, Council for High Blood Pressure Research. Guidelines for the prevention of stroke in women: a statement for healthcare professionals from the American Heart Association/American Stroke Association. Stroke. 2014 May;45(5):1545-88. [449 references] PubMed

Adaptation

Not applicable: The guideline was not adapted from another source.

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Financial Disclosures/Conflicts of Interest

The American Heart Association makes every effort to avoid any actual or potential conflicts of interest that may arise as a result of an outside relationship or a personal, professional, or business interest of a member of the writing panel. Specifically, all members of the writing group are required to complete and submit a Disclosure Questionnaire showing all such relationships that might be perceived as real or potential conflicts of interest.

See the original guideline document for a listing of Writing Group Disclosures.

Guideline Endorser(s)

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Guideline Status This is the current release of the guideline. Guideline Availability Electronic copies: Available from the Stroke Journal Web site Print copies: Available from the American Heart Association, Public Information, 7272 Greenville Ave, Dallas, TX 75231-4596; Phone: 800-242-8721. **Availability of Companion Documents** The following are available: Bushnell C, McCullough L. Stroke prevention in women: synopsis of the 2014 American Heart Association/American Stroke Association guideline. Ann Intern Med. 2014 Jun 17;160(12):853-857. Electronic copies: Available from the Annals of Internal Medicine Web site • Preventing stroke in women. Continuing Medical Education. Available from the Annals of Internal Medicine Web site **Patient Resources** The following are available: Preventing stroke in women-frequently asked questions. Available from the American Heart Association (AHA) Web site • Women face higher risk of stroke. Infographic. Available from the AHA Web site Please note: This patient information is intended to provide health professionals with information to share with their patients to help them better understand their health and their diagnosed disorders. By providing access to this patient information, it is not the intention of NGC to provide specific medical advice for particular patients. Rather we urge patients and their representatives to review this material and then to consult with a licensed health professional for evaluation of treatment options suitable for them as well as for diagnosis and answers to their personal medical questions. This patient information has been derived and prepared from a guideline for health care professionals included on NGC by the authors or publishers of that original guideline. The patient information is not reviewed by NGC to establish whether or not it accurately reflects the original guideline's content. **NGC Status** This NGC summary was completed by ECRI Institute on March 24, 2014. The information was verified by the guideline developer on April 28, 2014. Copyright Statement

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